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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/764,730	01/26/2004	Hans Konrad Muller-Hermelink	50308/009002	8646

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EXAMINER	
PHAM, AUDREY S	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 11/17/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/764,730	MULLER-HERMELINK ET AL.	
	Examiner	Art Unit	
	Audrey S. Pham	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-57 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) 1-57 are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Re: Muller-Hermelink *et al.*

Claims 1-57 are pending.

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-2, 5-7, 9, 39-40, drawn specifically to an isolated polypeptide that binds to a neoplastic cell wherein said polypeptide comprises SEQ ID NO: 2, a pharmaceutical composition, and a diagnostic agent, classified in class 530, subclass 350.

II. Claims 1, 3-7, 9, 39-40, drawn specifically to an isolated polypeptide that binds to a neoplastic cell wherein said polypeptide comprises SEQ ID NO: 4, a pharmaceutical composition, and to a diagnostic agent, classified in class 530, subclass 350.

III. Claims 1, 3, 5-9, 39-40, drawn specifically to a functional fragment of an antibody comprising specific fragments of SEQ ID NOs: 3 and 4, a pharmaceutical composition, and to a diagnostic agent, classified in class 530, subclass 387.1.

IV. Claims 10-11, 15-21, drawn to an isolated nucleic acid molecule comprising nucleic acids 31-45, 88-138 and 235-264 of SEQ ID NO: 1, to a vector thereof, to an isolated cell comprising said vector, and to a method of producing a polypeptide, classified in class 536, subclass 23.1.

V. Claims 12-13, 15-16, drawn to an isolated nucleic acid comprising nucleic acids 49-96, 142-162 and 259-285 of SEQ ID NO: 3, to a vector thereof and to an isolated cell comprising said vector, classified in class 536, subclass 23.1.

VI. Claims 14-16, drawn to an isolated nucleic acid molecule comprising the sequence of SEQ ID NO: 5, a vector thereof and to an isolated cell comprising said vector, classified in class 536, subclass 23.1.

VII. Claims 22-30, drawn to a method of diagnosing a neoplasm or a pre-cancerous lesion in a mammal comprising contacting a cell or tissue sample derived from said mammal with the purified polypeptide wherein said isolated polypeptide comprises amino acids 11-15, 30-46 and 79-88 of SEQ ID NO: 2 and detecting whether said purified polypeptide specifically binds to said cell or tissue, classified in class 435, subclass 7.23.

VIII. Claims 31-32, 36-38, drawn to a method of treating a proliferative disorder in a mammal said method comprising the step of contacting a cell with the purified polypeptide comprising amino acids 11-15, 30-46 and 79-88 of SEQ ID NO: 2, wherein binding of said purified polypeptide to said cell results in the induction of apoptosis of said cell, classified in class 424, subclass 184.1.

IX. Claims 31-35, drawn to a method of treating a proliferative disorder in a mammal said method comprising the step of contacting a cell with the purified polypeptide wherein said polypeptide is an antibody, classified in class 424, subclass 130.1.

X. Claims 41-50, drawn to an isolated polypeptide wherein said polypeptide comprises an amino acid sequence consisting of amino acids 469-518 of SEQ ID NO: 6 or amino acids 739-748 of SEQ ID NO: 6, to a pharmaceutical composition, to a diagnostic agent, and to a method of producing said polypeptide, classified in class 530, subclass 300.

XI. Claims 51-53, drawn to a method of inducing a tumor-specific immune response comprising contacting a mammal with an isolated polypeptide comprising the amino acid sequence of SEQ ID NO: 6 or a fragment thereof comprising amino acids 469-518 of SEQ ID NO: 6 or amino acids 739-748 of SEQ ID NO: 6, classified in class 435, subclass 184.1.

XII. Claim 54, drawn to a method of producing an isolated polypeptide comprising the sequence of SEQ ID NO: 6 or a fragment thereof comprising contacting a cell with a vector comprising a nucleic acid sequence that is substantially identical to SED ID NO: 5 and isolating the polypeptide expressed by said cell, classified in class 435, subclass 69.1.

XIII. Claims 55-57, drawn to a method of identifying a candidate therapeutic compound comprising contacting a cell expressing a polypeptide comprising the amino acid sequence of SEQ ID NO: 6 or a fragment thereof comprising amino acids 469-518 of SEQ ID NO: 6 or amino acids 739-748 of SEQ ID NO: 6 with a test compound and determining whether said test compound induces apoptosis of said cell, classified in class 435, subclass 4.

The inventions are distinct, each from the other for the following reasons:

The inventions of groups I-VI, X and the methods of groups VII-IX, XI-XIII are related as products and processes of use. The inventions can be shown to be distinct if one of the following can be shown: (i) the process for using the product as claimed can be practiced with another materially different product or (ii) the product as claimed can be used in a materially different process of using that product [*See* MPEP § 806.05(h)]. In the instant case, the nucleic acid molecules, as claimed, can be used in a materially different process such as in methods of developing binding assays, methods of purification, or methods of making said nucleic acid molecules. Likewise, the polypeptides, as claimed, can be used in materially different methods such as in methods of developing vaccines, methods of treating cancer or methods of developing a therapeutic inhibitor.

The inventions of groups I-VI, X encompass multiply distinct and independent products that encompass different functional as well as structural formulas. Groups I-II and X encompass polypeptides. Groups IV-VI encompass polynucleotides and group III encompasses an antibody. The polypeptides of groups I-II and X are composed of amino acids whereas the polynucleotides of group IV-VI are composed of nucleic acids. Each of these molecules is structurally distinct. The antibody of group III includes, for example, IgG molecules which comprise 2 heavy and 2 light chains containing constant and variable regions, and including framework regions which act as a scaffold for the 6 complementarily determining regions (CDRs). Each of these groups represent separate and distinct chemical products which are made by materially different methods, and are used in materially different methods which have different modes of operation, different functions and different effects. They have separate statuses in the art as shown by their different classifications. Any relationship between a polynucleotide and polypeptide is dependent upon the information provided by nucleic acid sequence open reading frame as it corresponds to the primary amino acid sequence of the encoded polypeptide. Therefore, the polypeptides and polynucleotides are patentably distinct. Furthermore, the polypeptide of group I is distinct from the polypeptide of group II, each has a different amino acid makeup, a different 2- and 3-dimensional folds, and different biochemical features such that one cannot be interchanged for the other. Likewise, each nucleic acid molecule of groups IV-VI is distinct from the other nucleic acid molecules. Searching the inventions of all groups would impose a serious search burden since a search result of one group could not be used to determine the patentability of the other groups.

The inventions of groups VII-IX, XI-XIII are materially distinct methods, which differ at least in objectives, method steps and reagents. Specifically, group VII is drawn to a method of diagnosing a neoplasm; group VIII-IX are drawn to methods of treating a proliferative disorder; group XI is drawn to a method of inducing a tumor-specific immune response; group XII is drawn to a method of producing an isolated polypeptide; and group XIII is drawn to a method of identifying a candidate therapeutic compound. Each invention differs in the reagents and steps they use to achieve different objectives. For example, the invention of group VII comprises of contacting a cell or tissue with a purified polypeptide of

SEQ ID NO: 2 and detecting whether said polypeptide specifically binds to said cell or tissue; but group XI comprises of contacting a cell or tissue with a fragment of purified polypeptide of SEQ ID NO: 6. Searching all of the groups with all of the different reagents, steps or objectives would invoke a serious search burden.

These inventions are distinct for the reasons given above and they have acquired separate statuses in the art as shown by their different classifications. The search required for one group is not required for the other groups and vice versa. For these reasons, restriction for examination purposes as indicated is proper.

Species Election

One or more of the above invention groups contain multiple generic claims that include a plurality of alternatively usable substances or members. These alternative limitations are independent or distinct inventions such that they do not share a common utility or share a substantial structural feature disclosed as being essential to that utility. Because they are not so closely related, a search and examination of the entire claim cannot be made without undue burden. The members of the alternative groupings are described in the following:

Groups I, VII (Claims 6, 48) are generic to a plurality of disclosed patentably distinct species comprising the following neoplastic cells: Barrett's tumors, esophagus, stomach, intestine, rectum, liver, gallbladder, pancreas, lungs, bronchi, breast, cervix, prostate, heart, ovary, uterus, and not by a normal cell of the same tissue type

The neoplastic cells of the above species represent separate and distinct cells that differ at least in etiology, pathology, and mechanisms. As such, each species would require different searches and the consideration of different patentability issues.

Alternatively, group I, VII (Claims 7, 47) are generic to a plurality of disclosed patentably distinct species comprising the following pre-cancerous lesions: dysplasia of the gastric mucosa, interstitial metaplasia of the stomach, inflammation of the gastric mucosa

associated with bacteria Helicobacter pylori, tubular and tubulovillous adenomas of the stomach, tubular adenoma of the colon, villous adenoma of the colon, dysplasia in ulcerative colotis, Barrett's dysplasia, Barrett's metaplasia of the esophagus, cervical intraepithelial neoplasia I, cervical intraepithelial neoplasia II, cervical intraepithelial neoplasia III, squamous epithelial metaplasia, squamous epithelial dysplasia of the bronchus, low grade and high grade prostrate intraepithelial neoplasia (PIN), breast ductal carcinoma *in situ* (D-CIS), breast lobular carcinoma *in situ* (L-CIS) and not by normal cells of the same tissue type.

The precancerous lesions of the above species represent separate and distinct lesions that differ at least in etiology, pathology, and mechanisms. As such, each species would require different searches and the consideration of different patentability issues.

Group V (Claim 23) is generic to a plurality of disclosed patentably distinct species comprising the following tissues: Barrett's tumors, esophagus, stomach, intestine, rectum, liver, gallbladder, pancreas, lungs, bronchi, breast, cervix, prostate, heart, ovary, uterus, dysplasia of the gastric mucosa, interstitial metaplasia of the stomach, inflammation of the gastric mucosa associated with bacteria Helicobacter pylori, tubular and tubulovillous adenomas of the stomach, tubular adenoma of the colon, villous adenoma of the colon, dysplasia in ulcerative colotis, Barrett's dysplasia, Barrett's metaplasia of the esophagus, cervical intraepithelial neoplasia I, cervical intraepithelial neoplasia II, cervical intraepithelial neoplasia III, squamous epithelial metaplasia, squamous epithelial dysplasia of the bronchus, low grade and high grade prostrate intraepithelial neoplasia (PIN), breast ductal carcinoma *in situ* (D-CIS), and breast lobular carcinoma *in situ* (L-CIS).

The tissue types of the above species represent separate and distinct tissues that differ at least in etiology, pathology, and mechanisms. As such, each species would require different searches and the consideration of different patentability issues.

Upon election of group I-III, VII, or X, Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits. Please note this is a provisional election to which the claims shall be restricted if no generic claim is finally held

to be allowable. Additionally, if group I-III or VII is elected Applicant must elect a neoplastic cell or a pre-cancerous lesion, not both.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

Rejoining Claims

NOTE:

The Examiner has required restriction between product and process claims. Where Applicant elects claim(s) directed to a product and the product claim(s) is/are subsequently found allowable, the withdrawn process claim(s) that depend(s) from or otherwise include all the limitations of the allowable product claim(s) will be rejoined in accordance with the provisions of MPEP § 821.04. Process claims that depend from or otherwise include all the limitations of the patentable product will be entered as a matter of right if an amendment is presented prior to a final rejection or allowance, whichever is earlier. Amendment submitted after final rejection is

governed by 37 CFR 1.116; amendment submitted after allowance is governed by 37 CFR 1.312.

In the event of a rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claim(s) and process claim(s) may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the withdrawn process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Inventorship Amendment

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended to be in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request, as set forth in 37 CFR 1.48(b), and by a processing fee, as set forth in 37 CFR 1.17(i).

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Audrey S. Pham whose telephone number is (571) 272-3323. The examiner can normally be reached during the hours of 8:30 AM - 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew, can be reached during business hours at the telephone number: (571) 272-0787. The fax number for the organization, where this application or proceeding is assigned, is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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PRIMARY EXAMINER